Extracts of biological materials, including but not limited to cells, tissues, organs, and tumors may also be electroprocessed. Collagen has been electrospun to produce a repeating, banded pattern observed with electron microscopy. This banded pattern is typical of collagen fibrils produced by natural processes (i.e. banded pattern is observed in collagen when it is produced by cells). In some embodiments, collagen is electrospun such that it has a 65 nm banding pattern.

It is to be understood that these electroprocessed materials may be combined with other materials and/or substances in forming the compositions of the present invention. For example, an electroprocessed peptide may be combined with an adjuvant to enhance immunogenicity when implanted subcutaneously. As another example, an electroprocessed collagen matrix, containing cells, may be combined with an electroprocessed biologically compatible polymer and growth factors to stimulate growth and division of the cells in the collagen matrix.

Synthetic materials include any materials prepared through any method of artificial synthesis, processing, or manufacture. The synthetic materials are preferably biologically compatible for administration in vivo or in vivo. Such polymers include but are not limited to the following: poly(urethanes), poly(siloxanes) or silicones, poly(ethylene), poly(vinyl pyrrolidone), poly(2-hydroxy ethyl methacrylate), poly(N-vinyl pyrrolidone), poly(methyl methacrylate), poly(vinyl alcohol), poly(acrylic acid), polyacrylamide, poly(ethylene-co-vinyl acetate), poly(ethylene glycol), poly(methacrylic acid), polylactic acid (PLA), polyglycolic acids (PGA), poly(lactide-co-glycolides) (PLGA), nylons, polyamides, polyanhydrides, poly(ethylene-co-vinyl alcohol) (EVOH), polycaprolactone, poly(vinyl acetate) (PVA), polyvinylhydroxide, poly(ethylene oxide) (PEO) and polyorthoesters or any other similar synthetic polymers that may be developed that are biologically compatible. Some preferred synthetic matrix materials include PLA, PGA, copolymers of PLA and PGA, polycaprolactone, poly(ethylene-co-vinyl acetate), (EVOH), PVA, and PEO. Matrices can be formed of electrospun fibers, electroaerosol, electrosprayed, or electrosputtered droplets, or a combination of the foregoing.

In embodiments in which natural materials are used, those materials can be derived from a natural source, synthetically manufactured, or manufactured by genetically engineered cells. For example, genetically engineered proteins can be prepared with specific desired sequences of amino acids that differ from the

natural proteins. In one illustrative embodiment, desirable sequences that form binding sites on a collagen protein for cells or peptides can be included in higher amounts than found in natural collagen.

By selecting different materials, or combinations thereof, many characteristics of the electroprocessed material can be manipulated. The properties of the matrix comprised of electroprocessed material and a substance may be adjusted. As discussed in greater detail below, electroprocessed materials themselves can provide a therapeutic effect when applied. In addition, selection of matrix materials can affect the permanency of an implanted matrix. For example, matrices made of fibrin will degrade more rapidly while matrices made of collagen are more durable and synthetic matrix materials are more durable still. Use of matrices made of natural materials such as proteins also minimize rejection or immunological response to an implanted matrix. Accordingly selection of materials for electroprocessing and use in substance delivery is influenced by the desired use. In one embodiment, a skin patch of electroprocessed fibrin or collagen combined with healing promoters and anti-rejection substances may be applied to the skin and may subsequently dissolve into the skin. In another embodiment, an implant for delivery to bone may be constructed of materials useful for promoting bone growth, osteoblasts and hydroxyapatite, and may be designed to endure for a prolonged period of time.

Synthetic components, such as biocompatible substances can be used to modulate the release of materials from an electroprocessed composition. For example, a drug, or series of drugs or other materials to be released in a controlled fashion can be electroprocessed into a series of layers. One layer is composed of PGA plus a drug, the next layer PLA plus a drug, a third layer is composed of polycaprolactone plus a drug. The layered construct can be implanted, and as the successive layers dissolve or breakdown, the drug (or drugs) is released in turn as each successive layer erodes. Unlayered structures can also be used, and release is controlled by the relative stability of each component of the construct. Another advantage of the synthetic materials is that different solvents can be used. This can be important for the delivery of some materials. For example, a drug may be soluble in some organics, and using synthetics increases the number of materials that can be electroprocessed. The breakdown of these synthetic materials can be tailored and regulated in ways that are not available to natural materials. The synthetics are usually not subject to

enzymatic breakdown, and many spontaneously undergo hydrolysis. In addition to these characteristics, substances can be released from electroprocessed materials in response to electrical, magnetic and light based signals. Polymers that are sensitive to such signals can be used, or the polymers may be derivatized in a way to provide such sensitivity. These properties provide flexibility in making and using electroprocessed materials designed to deliver various substances, in vivo and in vitro.

In some embodiments of the present invention, the electroprocessed material itself provides a therapeutic effect. For example, in some embodiments electroprocessed collagen promotes cellular infiltration and differentiation, so an electroprocessed collagen matrix alone assists with healing. The P-15 site, a 15 amino acid sequence within the collagen molecule, promotes osteoblasts to produce and to secrete hydroxyapatite, a component of bone. Another example of specific sites and sequences within collagen molecules that can be manipulated and processed in a similar fashion includes the RGD binding sites of the integrin molecule. The RGD site is a sequence of three amino acids (Arg-Gly-Asp) present in many matrix materials that serves as a binding site for cell adhesion. It is recognized and bound, for example, by integrins. In addition, electroprocessed materials can be enriched with specific desired sequences before, during, or after electroprocessing. Sequences can be added in linear or other forms. In some embodiments, the RGD sequences are arranged in a cyclic form referred to as cycloRGD.

An electroprocessed material, such as a matrix, can also be composed of specific subdomains of a matrix constituent and can be prepared with a synthetic backbone that can be derivatized. For example, the RGD peptide sequence, and/or a heparin binding domain and/or other sequences, can be chemically coupled to synthetic materials. The synthetic polymer with the attached sequence or sequences can be electroprocessed into a construct. This produces a matrix with unique properties. In these examples the RGD site provides a site for cells to bind to and interact with the matrix. The heparin-binding site provides a site for the anchorage of peptide growth factors to the synthetic backbone. Angiogenic peptides, genetic material, growth factors, cytokines, enzymes and drugs are other non-limiting examples of substances that can be attached to the backbone of an electroprocessed material to provide functionality. Peptide side chains may also be used to attach molecules to functional groups on polymeric backbones.